Please substitute the enclosed sections entitled "5.3 EXAMPLE 3 – DEVELOPMENT AND TESTING OF RIBOZYME TARGETING A_{2B} ADENOSINE RECEPTOR mRNA" for the corresponding section originally submitted with the application as filed.

Please substitute the enclosed TABLE 4, TABLE 5 and TABLE 6 for the corresponding tables originally submitted with the application as filed.

After page 111, please insert the Sequence Listing that is enclosed herewith.

REMARKS

The above amendments are for the purpose of correcting the drawing descriptions, correcting some of the tables, and inserting the sequence listing.

Should any fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason, the Assistant Commissioner is authorized to deduct said fees from Williams, Morgan & Amerson, P.C. Deposit Account No. 50-0786/4300.014100.

Please date stamp and return the accompanying postcard to evidence receipt of these documents.

Respectfully submitted,

Date: September 12, 2001

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3. BRIEF DESCRIPTION OF THE DRAWINGS

The following drawings form part of the present specification and are included to further demonstrate certain aspects of the present invention. The invention may be better understood by reference to the following description taken in conjunction with the accompanying drawings, in which like reference numerals identify like elements, and in which:

FIG. 1 shows adenosine, acting through its type A_2 receptor, can act to increase oxygen supply via two paths. During acute hypoxia, adenosine acts on smooth muscle cells, resulting in vasodilation (A_{2A}). With chronic ischemia, adenosine acts as an angiogenic agent by exerting a mitogenic effect on microvascular endothelial cells (in HREC, A_{2B}; see below). It is this latter effect that can be interfered with in an attempt to develop a pharmacological therapy for neovascular diseases. A distinct receptor subtype that mediates solely the mitogenic effect of adenosine would allow the targeting of a selective antagonist against that receptor subtype, without preventing the vasodilation mediated by the A_{2A} receptor;

FIG. 2A shows HREC proliferation after stimulation with NECA alone or in combination with a blocking antibody to VEGF. Open bars are results after 24 hr of exposure; filled bars are results after 48 hr. (*), significantly different from 10 μM NECA alone for the respective exposure time by ANOVA ($p < 0.05$). Also shown are control cells exposed to VEGF alone or in combination with anti-VEGF to demonstrate the efficacy of the antibody;

FIG. 2B shows VEGF content in conditioned medium from HREC after stimulation with NECA in the presence or absence of sense or antisense oligonucleotides homologous to human A_{2B} adenosine receptor or to human VEGF. Assay duration was 48 hr. A_{2B} antisense treatment reduces the amount of VEGF protein secreted in response to NECA to levels equaling or exceeding the reduction evident by VEGF antisense treatment;

FIG. 3A and **FIG. 3B** show NECA, at the concentrations indicated in the legends, induces a transient activation of ERK/MAPK in HREC that peaks at 5 min and desensitizes by 20 min after exposure. HREC were serum-starved for 24 hr and pre-treated for 20 min with 1 U/mL adenosine deaminase prior to adding NECA. Activated ERK/MAPK was visualized on Western blots by enhanced chemiluminescence using EC10 monoclonal antibody;

FIG. 4A, **FIG. 4B** and **FIG. 4C** show the A_1-selective agonist CPA stimulates ERK/MAPK phosphorylation in HREC, however the A_{2A}-selective agonist CGS did not activate ERK/MAPK;

FIG. 5 shows HREC were pretreated for 30 min with the MEK inhibitor PD98059 or the PKA inhibitor H-89 and stimulated with NECA for 5 min. PD98059 inhibited ERK activation, while H-89 increased basal ERK activation. H-89 did not block NECA-stimulated ERK activation, suggesting that PKA is not involved in signaling from the adenosine receptor to ERK. The non-selective adenosine receptor antagonist XAC decreased ERK activation by high concentrations of NECA, but modestly increased ERK activation in control conditions and in response to 1 and 10 nM NECA. In contrast, PD98059 did not alter CREB, whereas both H-89 and XAC blocked NECA-induced CREB activation. These data indicate that NECA results in ERK activation independent of the cAMP response;

FIG. 6 shows both Enprofylline and JW V-108 antagonize activation of p42 and p44 ERK/MAP kinase by NECA. HRECs were serum-starved for 24 hr and pre-treated with adenosine deaminase (ADA, 1 U/mL) for 20 min, incubated with the antagonists in the presence of ADA for 10 min. NECA (1 nM-10 μM, 10 min) was used to activate ERK. ERK activation was analyzed by Western blot using the E10 monoclonal antibody, which recognizes the phosphorylated (active) form of the enzyme;

FIG. 7A, **FIG. 7B** and **FIG. 7C** show a schematic representation (FIG. 7A) of the A_{2B} adenosine receptor ribozyme showing the nucleotide sequence of the recognition arms (SEQ ID NO:1), as well as the complementary sequence of the synthetic target (SEQ ID NO:2). Cleavage of this target by the ribozyme is shown in the autoradiogram (FIG. 7B), demonstrating the cleavage kinetics. Band densities of cleaved *vs.* intact target were plotted as percent cleaved (FIG. 7C). The A_{2B} receptor ribozyme cleaves nearly 90% of target in a 1:1 molar ratio by 60 min;

FIG. 8A and **FIG. 8B** show A_{2B} adenosine receptor ribozyme reduces NECA-stimulated VEGF synthesis and cell proliferation in HREC. Cells were stimulated with 10 μmol/L NECA alone (◆), or NECA plus 1 μmol/L of either a mixed 37-mer oligoribonucleotide (sham, ■) or A_{2B} ribozyme (▲). Both the amount of VEGF secreted into the medium (top) and the degree of proliferation (bottom) were decreased by the ribozyme, and not by the sham oligonucleotide control; and

FIG. 9 shows adenosine receptor antagonists reduce the degree of retinal neovascularization in the mouse pup model of oxygen-induced retinopathy. Daily IP injections of antagonists (30 mg/Kg body weight) resulted in a 54% to 70% reduction compared to untreated controls. The

number of eyes examined for each condition was at least 16. *Significantly different ($p < 0.05$) from uninjected.

FIG. 10 shows the number of neovascular nuclei counted per eye section for both the uninjected and AAV-IGF1R Rz1 injected eyes. Helex IV is at least 6 bases in length. The underlined bases can be any RNA tetraloop of the form $^{5'}$GNRA$^{3'}$ or UUCG, where N is any nucleotide and R is G or A. N can be any ribonucleotide (A, C, G or U) and N' is the complementary nucleotide. Y is a pyrimidine. H is any nucleotide but guanosine (A, C or U). B is any nucleotide but adenosine (G, C or U). V is the complement of B (G, C or A).

FIG. 11 shows a schematic illustration of a representative hairpin ribozyme molecule of the present invention (SEQ ID NO:105, SEQ ID NO:106). In particular, FIG. 11 shows a general hammerhead ribozyme structure. The italicized positions are constant. The stem may be any 4 or 5 base double stranded helix with a $^{5'}$G-C$^{3'}$ base pair at the top of the stem as drawn. Helix IV is at least 6 bases in length. The underlined bases can be any RNA tetraloop of the form $^{5'}$GNRA$^{3'}$ or UUCG, where N is any nucleotide and R is G or A. N can be any ribonucleotide (A, C, G or & and N' is the complementary nucleotide. Y is a pyrimidine. H is any nucleotide but guanosine (A, C or U). B is any nucleotide but adenosine (G, C or U). V is the complement of B (G, C or A).

FIG. 12 shows a schematic illustration of a representative hammerhead ribozyme molecule of the present invention (SEQ ID NO:107). The sequences of the arms may vary, as shown in Tables 4-8. The italicized positions are constant. The stem may be any 4 or 5 base double stranded helix with a $^{5'}$G-C$^{3'}$ base pair at the top of the stem as drawn. Underlined nucleotides in loop may be $^{5'}$UUCG$^{3'}$ or $^{5'}$GNRA$^{3'}$, where N is any nucleotide and R is a purine nucleotide.

5.2.4 ADENOSINE A_{2B} RECEPTOR REQUIRED FOR HREC ERK ACTIVATION

NECA (1 nmol/L – 10 μmol/L) induced a transient activation of ERK which peaked at 5 min and desensitized within 20 min. The rate of desensitization was dependent on NECA concentration since higher doses of NECA produced a more rapid desensitization (FIGS. 3A-3B). The A_1-selective agonist CPA was also capable of stimulating ERK (FIGS. 4A-4C), however the A_{2A}-selective agonist CGS did not activate ERK. In order to determine the intracellular signaling pathways activated by NECA that regulate ERK activity, we pretreated cells for 30 min with the ERK/MPAK kinase (MEK) inhibitor PD98059 or the PKA inhibitor H-89 and stimulated with NECA for 5 min. PD98059 abolished ERK activation, while H-89 increased basal ERK activation (FIG. 5). H-89 did not block NECA-stimulated ERK activation, suggesting that PKA is not involved in signaling from the adenosine receptor to ERK. The non-selective adenosine receptor antagonist XAC decreased ERK activation by high concentrations of NECA, but modestly increased ERK activation in control conditions and in response to 1 and 10 nM NECA. Interestingly, prolonged activation with NECA in the presence of XAC or SCH and CPX reduced the rate of ERK desensitization, suggesting that adenosine receptors are involved in both activation and desensitization of ERK.

Phosphorylation of cAMP response element binding protein (CREB) at Ser^{133} was examined following NECA stimulation in order to determine whether activation of cAMP pathways by NECA occurred independently of ERK activation. Cells were pretreated with PD98059 or H-89 and assayed for active CREB by western blot. PD98059 did not alter CREB activation, however both H-89 and XAC blocked CREB phosphorylation. These data indicate that ERK activation by NECA occurs independently of the cAMP response (FIG. 5).

Enprofylline and JW V108 exhibit greater selectivity for the A_{2B} receptor. Cells were pre-treated with both antagonists for 10 min and stimulated with increasing concentrations of NECA. Enprofylline completely abolished ERK activation, while JW V108 inhibited ERK activation at all concentrations except for 10 μM. These data suggest that ERK activation occurs through both the A_{2B} and A_1 receptors, but not the A_{2A} receptor (FIG. 6). These data support a role for adenosine in the activation of ERK that may then induce the phosphorylation of HIF 1-α.

5.3 EXAMPLE 3 – DEVELOPMENT AND TESTING OF RIBOZYME TARGETING A_{2B} ADENOSINE RECEPTOR mRNA

The cleavage site of the A_{2B} antisense, between nucleotides 183 and 184, was demonstrated to be accessible within the secondary structure of the native mRNA by the antisense studies. A hammerhead ribozyme designed to cleave this message was then synthesized along with a 14-nucleotide target sequence (FIG. 7A). This target was end-labeled in a standard kinase reaction with ^{32}P, then incubated along with ribozyme (1:1 molar ratio) for 1, 2, 3, 4, 5, 10, 30, 60, 120 and 180 min. Nearly 90% of target was cleaved by 60 min (FIG. 7C), demonstrating the efficacy and rapid action of this ribozyme in a cell-free assay system. The ribozyme's effects on HREC proliferation and VEGF synthesis in response to adenosine receptor activation was examined. HRECs were plated in serum-free medium overnight to adhere and make them quiescent. Unattached cells were then removed by washing with Hank's balanced salt solution (HBSS). The cells were then incubated with 1 U/mL adenosine deaminase (ADA) for 20 min, after which was added either medium alone, 1 μmol/L A_{2B} receptor ribozyme, or 1 μmol/L of a synthetic mixed oligonucleotide of the same length as the ribozyme, all of which contained 10 μmol/L NECA. Cells were then incubated for a total of seven days. Sampling occurred every 24 hr as follows. Conditioned medium was collected and stored at –70°C until the end of the assay, after which it was analyzed for VEGF using a commercially available ELISA. The cells were enzymatically dissociated from the wells and counted using a Coulter counter. These latter results were then used to normalize the VEGF data to a constant cell number. FIGS. 8A-8B show that cells treated with ribozyme express up to 60% less VEGF protein in response to NECA than do either untreated cells or cells treated with sham oligonucleotide. Similarly, these same cells exhibited a 50% reduction in proliferation 7 days after NECA stimulation when exposed to ribozyme compared to control.

TABLE 4

ILLUSTRATIVE HAIRPIN RIBOZYME TARGETS OF THE PRESENT INVENTION

RIBOZYME	SEQUENCE			SEQ ID NO:	REFERENCE
		Cleavage site			
	HelixII		Helix I		
ROD OPSIN mRNA-SPECIFIC:					
P23L target:	acgc	a gcc	**u**cuucg-3'	SEQ ID NO:3	Berson *et al.*, 1991
Ribozyme arms:	ugcg	aaga	agaagc-5'	SEQ ID NO:108	
F45L target:	acau	g **g**uu	cugcug	SEQ ID NO:4	Sung *et al.*, 1991
Ribozyme arms:	ugug	aaga	gacgac	SEQ ID NO:109	
G51A target:	ugcu	g g**c**c	uucccc	SEQ ID NO:5	Macke *et al.*, 1993
Ribozyme arms:	acgg	aaga	aagggg	SEQ ID NO:110	
G51G target:	ugcu	g g**u**c	uucccc	SEQ ID NO:6	Dryja *et al.*, 1991
Ribozyme arms:	acgg	aaga	aagggg	SEQ ID NO:111	
P53R target:	gcug	g gcu	ucc**g**gc	SEQ ID NO:7	Inglehearn *et al.*, 1992
Ribozyme arms:	cgac	aaga	aggccg	SEQ ID NO:112	

Q64stop target:	ucac	c guc	**u**agcac	SEQ ID NO:8	Macke *et al.*, 1993
Ribozyme arms:	agug	aaga	aucgug	SEQ ID NO:113	
G90D target:	aggu	g **g**cu	ucacca	SEQ ID NO:9	Sieving *et al.*, 1992
Ribozyme arms:	uccg	aaga	aguggu	SEQ ID NO:114	
G106W target	uuc**u**	g gcc	ccacag	SEQ ID NO:10	Sung *et al.*, 1991
Ribozyme arms:	aagg	aaga	gguguc	SEQ ID NO:115	
G114D target:	ugga	g g**a**c	uucuuu	SEQ ID NO:11	Vaithinathan *et al.*, 1994
Ribozyme arms:	accu	aaga	aagaaa	SEQ ID NO:116	
R135L target:	aucg	a g**uu**	guacgu	SEQ ID NO:12	Jacobson *et al.*, 1991
Ribozyme arms:	uagc	aaga	caugca	SEQ ID NO:117	
R135P target:	aucg	a g**c**c	guacgu	SEQ ID NO:13	Rodriguez *et al.*, 1993
Ribozyme arms:	uagc	aaga	caugca	SEQ ID NO:118	
P180A target:	acau	c **g**cc	gagggc	SEQ ID NO:14	Daiger *et al.*, 1995
Ribozyme arms:	ugug	aaga	cucccg	SEQ ID NO:119	

D190G target:	aauc	g **g**cu	acuaca	SEQ ID NO:15	Dryja *et al.*, 1991
Ribozyme arms:	uuag	aaga	ugaugu	SEQ ID NO:120	
H211R target:	ucgu	g guc	c**g**cuuc	SEQ ID NO:16	Macke *et al.*, 1993
Ribozyme arms:	agcg	aaga	gcgaag	SEQ ID NO:121	
H211P target:	ucgu	g guc	c**c**cuuc	SEQ ID NO:17	Macke *et al.*, 1993
Ribozyme arms:	agcg	aaga	gggaag	SEQ ID NO:122	
F220C target:	cauc	u guu	ucugcu	SEQ ID NO:18	Bunge *et al.*, 1993
Ribozyme arms:	guag	aaga	agacga	SEQ ID NO:123	
P347S target:	aggu	g gcc	**u**cggcc	SEQ ID NO:19	Dryja *et al.*, 1990
Ribozyme arms:	uccg	aaga	agccgg	SEQ ID NO:124	

TABLE 5

ILLUSTRATIVE HAMMERHEAD RIBOZYME TARGETS OF THE PRESENT INVENTION

RIBOZYME	SEQUENCE	SEQ ID NO:	REFERENCE
	Target reads 5' to 3' ribozyme reads 3' to 5'		
ROD OPSIN mRNA-SPECIFIC:			
P23H target:	gcc**a**cuu cgagua	SEQ ID NO:20	Berson *et al.*, 1991
ribozyme arms:	cgguga gcucau	SEQ ID NO:125	
P23L target:	gcc**u**cuu cgagua	SEQ ID NO:21	Dryja *et al.*, 1991
ribozyme arms:	cggaga gcucau	SEQ ID NO:126	
Q28H target:	caca**c**ua cuaccu	SEQ ID NO:22	Bunge *et al.*, 1993
ribozyme arms:	guguga gaggga	SEQ ID NO:127	
F45L target:	aug**g**uuc ugcuga	SEQ ID NO:23	Sung *et al.*, 1991
ribozyme arms:	uaccaa acgacu	SEQ ID NO:128	
L46R target:	auguuuc **g**gcuga	SEQ ID NO:24	Rodriguez *et al.*, 1993
ribozyme arms:	uacaaa ccgacu	SEQ ID NO:129	

G51R target:	ugcgcuu ccccau	SEQ ID NO:25	Dryja *et al.*, 1992
ribozyme arms:	acgcga ggggua	SEQ ID NO:130	
G51A target:	uggccuu ccccau	SEQ ID NO:26	Macke *et al.*, 1993
ribozyme arms:	accgga ggggua	SEQ ID NO:131	
G51V target:	uggucuu ccccau	SEQ ID NO:27	Dryja *et al.*, 1991
ribozyme arms:	accaga ggggua	SEQ ID NO:132	
P53R target:	ugggcuu ccgcau	SEQ ID NO:28	Inglehearn *et al.*, 1992
ribozyme arms:	acccga ggcgua	SEQ ID NO:133	
T58R target:	cuuccuc aggcuc	SEQ ID NO:29	Bunge *et al.*, 1993
ribozyme arms:	gaagga uccgag	SEQ ID NO:134	
T58R target:	caggcuc uacguc	SEQ ID NO:30	Bunge *et al.*, 1993
ribozyme arms:	guccga augcag	SEQ ID NO:135	
Q64stop target:	caccguc uagcac	SEQ ID NO:31	Macke *et al.*, 1993
ribozyme arms:	guggca aucgug	SEQ ID NO:136	

Q64stop target:	ccgucua gcacaa	SEQ ID NO:32	Macke *et al.*, 1993
ribozyme arms:	ggcaga cguguu	SEQ ID NO:137	
)68-71 target:	**ug**aacua cauccu	SEQ ID NO:33	Keen *et al.*, 1991
ribozyme arms:	acuuga guagga	SEQ ID NO:138	
V87D target:	gg**a**ccua gguggc	SEQ ID NO:34	Sung *et al.*, 1991
ribozyme arms:	ccugga ccaccg	SEQ ID NO:139	
G90D target:	gug**a**cuu caccag	SEQ ID NO:35	Sieving *et al.*, 1992
ribozyme arms:	cacuga gugguc	SEQ ID NO:140	
G106W target:	cgucuuc **u**ggccc	SEQ ID NO:36	Sung *et al.*, 1991
ribozyme arms:	gcagaa accggg	SEQ ID NO:141	
C110Y target:	caggau**a** caauuu	SEQ ID NO:37	Dryja *et al.*, 1992
ribozyme arms:	guccua guuaaa	SEQ ID NO:142	
G114D target:	agg**a**cuu cuuugc	SEQ ID NO:38	Vaithinathan *et al.*, 1994
ribozyme arms:	uccuga gaaacg	SEQ ID NO:143	

R135G target:	agggguacguggu	SEQ ID NO:39	Bunge *et al.*, 1993
ribozyme arms:	ucccca gcacca	SEQ ID NO:144	
R135L target:	aguggua cguggu	SEQ ID NO:40	Andreasson *et al.*, 1992
ribozyme arms:	ucacca gcacca	SEQ ID NO:145	
R135L target:	aguugua cguggu	SEQ ID NO:41	Jacobson *et al.*, 1991
ribozyme arms:	ucaaca gcacca	SEQ ID NO:146	
R135P target:	agccgua cguggu	SEQ ID NO:42	Rodriguez *et al.*, 1993
ribozyme arms:	ucggca gcacca	SEQ ID NO:147	
C140S target:	uggugucuaagcc	SEQ ID NO:43	Macke *et al.*, 1993
ribozyme arms:	accaca auucgg	SEQ ID NO:148	
P171L target:	accccuacucgcc	SEQ ID NO:44	Dryja *et al.*, 1991
ribozyme arms:	ugggga gagcgg	SEQ ID NO:149	
P171L target:	ccuacuc gccggc	SEQ ID NO:45	Dryja *et al.*, 1991
ribozyme arms:	ggauga cggccg	SEQ ID NO:150	

P171S target:	cacccuc acucgc	SEQ ID NO:46	Stone *et al.*, 1993
ribozyme arms:	guggga ugagcg	SEQ ID NO:151	
Y178C target:	gugcauc cccgag	SEQ ID NO:47	Farrar *et al.*, 1991
ribozyme arms:	cacgua gggcuc	SEQ ID NO:152	
P180A target:	guacauc gccgag	SEQ ID NO:48	Daiger *et al.*, 1995
ribozyme arms:	caugua cggcuc	SEQ ID NO:153	
C187Y target:	gcucgua uggaau	SEQ ID NO:49	Nathans *et al.*, 1993
ribozyme arms:	cgagca accuua	SEQ ID NO:154	
G188R target:	ucgugua gaaucg	SEQ ID NO:50	Dryja *et al.*, 1991
ribozyme arms:	agcaca cuuagc	SEQ ID NO:155	
D190G target	uggaauc ggcuac	SEQ ID NO:51	Dryja et al., 1991
ribozyme arms:	accuua ccgaug	SEQ ID NO:156	
D190Y target:	gaaucua cuacua	SEQ ID NO:52	Fishman *et al.*, 1992
ribozyme arms:	cuuaga gaugau	SEQ ID NO:157	

M207R target:	ca**g**guuc gugguc	SEQ ID NO:53	Farrar *et al.*, 1992
ribozyme arms:	guccaa caccag	SEQ ID NO:158	
H211R target:	cgugguc c**g**cuuc	SEQ ID NO:54	Macke *et al.*, 1993
ribozyme arms:	gcacca gcgaag	SEQ ID NO:159	
H211P target:	cgugguc c**c**cuuc	SEQ ID NO:55	Macke *et al.*, 1993
ribozyme arms:	gcacca gggaag	SEQ ID NO:160	
C264X target:	ccugaauc **ugggug**	SEQ ID NO:56	Vaithinathan *et al.*, 1993
ribozyme arms:	ggacuua acccac	SEQ ID NO:161	
P267L target:	ggugc**uc** uacgcc	SEQ ID NO:57	Fishman *et al.*, 1992
ribozyme arms:	ccacga augcgg	SEQ ID NO:162	
F220C target:	uaucauc u**g**uuuc	SEQ ID NO:58	Bunge *et al.*, 1993
ribozyme arms:	auagua acaaag	SEQ ID NO:163	
F220C target:	cu**g**uuuc ugcuau	SEQ ID NO:59	Bunge *et al.*, 1993
ribozyme arms:	gacaaa acgaua	SEQ ID NO:164	

C222R target:	ucuuuuc **c**gcuau	SEQ ID NO:60	Bunge *et al.*, 1993
ribozyme arms:	agacaa gcgaua	SEQ ID NO:165	
A292E target:	ag**a**guuc uuugcc	SEQ ID NO:61	Dryja *et al.*, 1993
ribozyme arms:	ucucaa aaacgg	SEQ ID NO:166	
Q344stop target:	cgagc**ua** gguggc	SEQ ID NO:62	Sung *et al.*, 1991
ribozyme arms:	gcucga ccaccu	SEQ ID NO:167	
P347S target:	uggccuc ggccua	SEQ ID NO:63	Dryja *et al.*, 1990
ribozyme arms:	accgga ccggau	SEQ ID NO:168	

RP1 mRNA-SPECIFIC:

R677stop target:	aaaaaauc **uu**gaca	SEQ ID NO:64	Pierce *et al.*, 1999
ribozyme arms:	uuuuuua aacugu	SEQ ID NO:169	

RDS/PERIPHERIN mRNA-SPECIFIC:

C118 target:	ggcucuc ugcu**uuc**	SEQ ID NO:65	Farrar *et al.*, 1991
ribozyme arms:	ccgaga acgaaag	SEQ ID NO:170	
R172Q target:	gguuuuc **a**ggacu	SEQ ID NO:66	Wells *et al.*, 1993
ribozyme arms:	ccaaaa uccuga	SEQ ID NO:171	

R172W target:	gguuuuu gggacu	SEQ ID NO:67	Wells *et al.*, 1993
ribozyme arms:	ccaaaa cccuga	SEQ ID NO:172	
P210R target:	guccguu ucagcu	SEQ ID NO:68	Jackson *et al.*, 1993
ribozyme arms:	caggca agucga	SEQ ID NO:173	
C214S target:	gcugcuc caaucc	SEQ ID NO:69	Keen and Inglehearn, 1996
ribozyme arms:	cgacga guuagg	SEQ ID NO:174	
P216L target:	aaucuua gcucgc	SEQ ID NO:70	Kajiwara *et al.*, 1991
ribozyme arms:	uuagaa cgagca	SEQ ID NO:175	
P219 target:	cuagcuc gcggcc	SEQ ID NO:71	Kajiwara *et al.*, 1991
ribozyme arms:	gaucga cgccgg	SEQ ID NO:176	

TABLE 6

ADDITIONAL ILLUSTRATIVE HAIRPIN RIBOZYME TARGETS OF THE PRESENT INVENTION

RIBOZYME	SEQUENCE			SEQ ID NO:	REFERENCE
	Cleavage site				
	HelixII ↓		Helix I		
RDS/PERIPHERIN mRNA-SPECIFIC:					
C118 target:	ucuc	u gcu	**uucugc**	SEQ ID NO:72	Farrar *et al.*, 1991
Ribozyme arms:	agag	aaga	aagacg	SEQ ID NO:177	
R172W target:	caac	g guu	uuu**g**gg	SEQ ID NO:73	Wells *et al.*, 1993
Ribozyme arms:	guug	aaga	aaaccc	SEQ ID NO:178	
P210R target:	cguc	c **g**uu	ucagcu	SEQ ID NO:74	Jackson *et al.*, 1993
Ribozyme arms:	gcag	aaga	agucga	SEQ ID NO:179	
C214S target:	cagc	u gcu	**c**caauc	SEQ ID NO:75	Keen and Inglehearn 1996
Ribozyme arms:	gucg	aaga	gguuag	SEQ ID NO:180	
P216L target:	ucu**u**	a gcu	cgccac	SEQ ID NO:76	Kajiwara *et al.*, 1991
Ribozyme arms:	agag	aaga	gcggug	SEQ ID NO:181	

P219 target:	uccu	a gcu	cgc**ggc**	SEQ ID NO:77	Kajiwara *et al.*, 1991
Ribozyme arms:	aggg	aaga	gcgccg	SEQ ID NO:182	